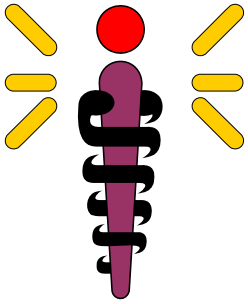
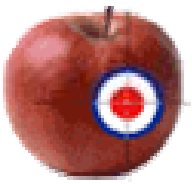
BIOLOGICS (WW)

NUTRITION Division





NUTRACEUTICALS MANUFACTURE

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MANUFACTURING of NUTRACEUTICALS & PHARMACEUTICALS

http://www.abpischools.org.uk/resources/manufacturing/index.asp

The **nutraceutical** and **pharmaceutical industry** provides medical practitioners with medicines - the tools of their trade. These have helped to raise our expectations of a long and healthy life. Their manufacture also contributes to the health of the economy through exports and providing a wide range of jobs.

Development and manufacture of new medicines and the **systems** that are used in their manufacture follow a pathway:

1. Introduction to the nutraceutical and pharmaceutical industry.
2. Systems in nutraceutical and pharmaceutical manufacture.
3. The development of a new medicine.
4. Primary manufacture.
5. Secondary manufacture.
6. Packaging.

What makes the neutraceutical and pharmaceutical manufacture different?

Introduction to the pharmaceutical industry:

Making a new medicine

- Research and Development (R&D).
- Primary manufacture - making the active ingredient.
- Secondary manufacture - formulating a medicine.

Formulating a medicine

Medicines can be given to a patient in many different forms. In this resource we will refer to all forms of dosage as the medicine. Examples of different medicines are:

- **Tablets and capsules.**
- **Injections.**
- **Topical medicines** (**creams and ointments**).
- **Inhalers**.
- **Syrups**.

Tablets and capsules

Tablets and capsules are useful because the dose is easily controlled and they can be stored without deteriorating. Some tablets are sucked or dispersed in water and swallowed (e.g. soluble aspirin). Gelatin capsules dissolve easily in the stomach, releasing the medicine which is absorbed from the gut into the bloodstream. Stomach acid destroys some medicines, so there are tablets coated with a substance which stops them dissolving until they reach the intestines.

Injections

Injections are a good way to deliver medicines to the place where they're needed. Medicines can also be injected directly into the bloodstream.

Emergency antidotes (e.g. antidotes to snake venom) are injected directly into the bloodstream for speed. Injections are also used for most types of **immunisation.**

Ointments, creams and powders

These are all applied directly to the skin in the affected area. They are called topical medicines. **Antiseptics** and **antifungals** (e.g. treatment for athlete's foot) may be used in this way.

Inhalers

Medicines can be breathed in using an inhaler. This delivers a fixed dose of medicine as a fine spray. The medicine is breathed straight into the lungs. People who have **asthma** use inhalers to get relief from breathing difficulties.

Syrups

Syrups are measured into a spoon and can be swallowed easily. They are often preferred by children, especially if they taste nice!

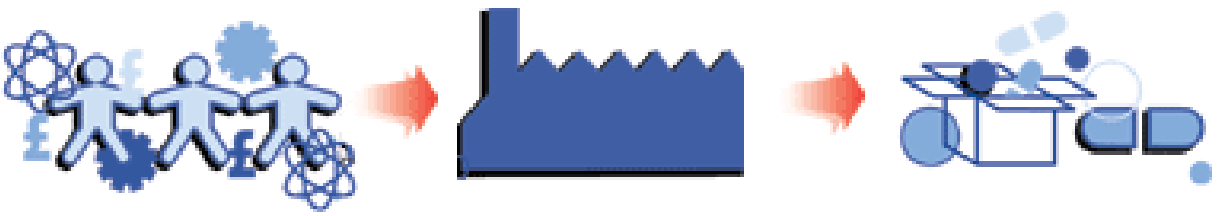
Patches

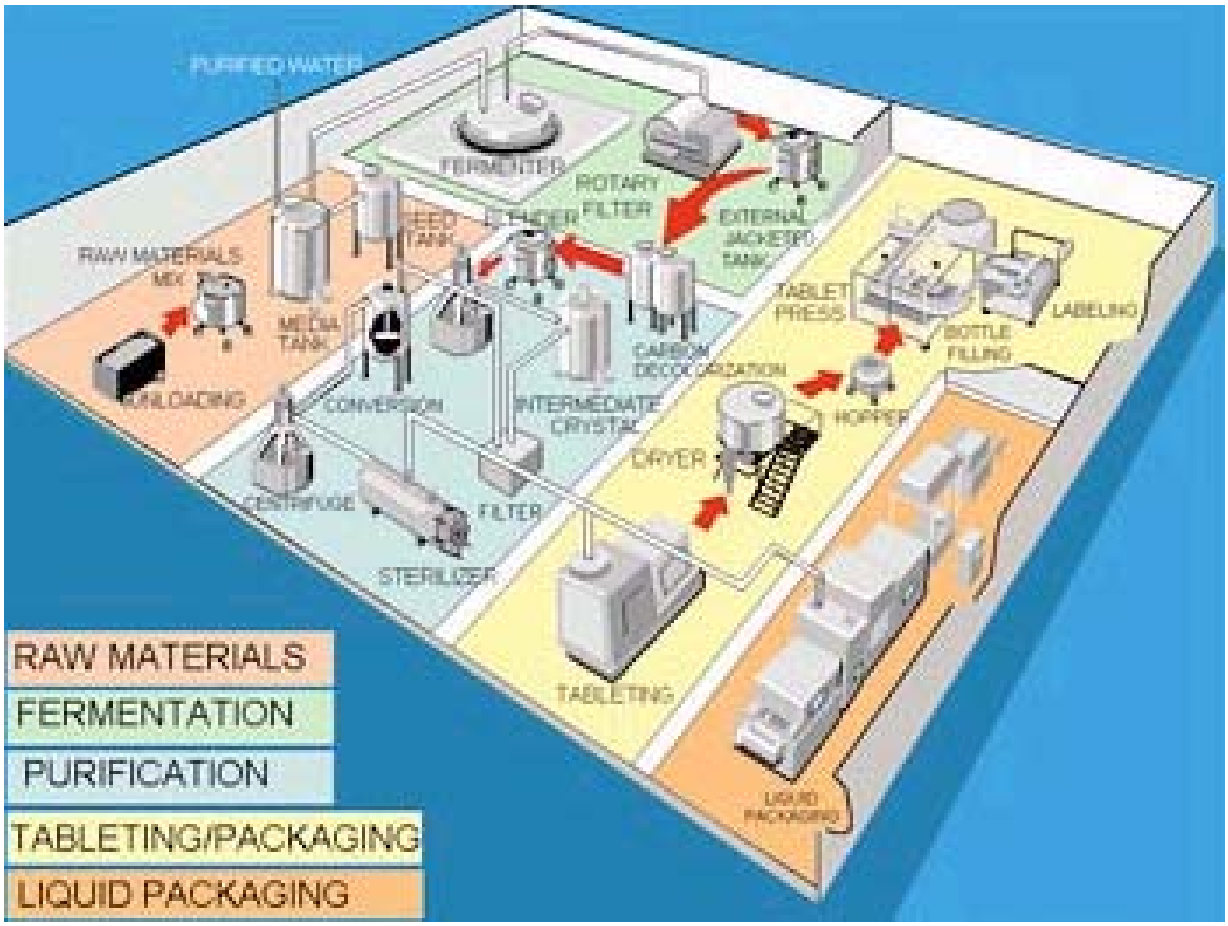
Some medicines are held in patches which are stuck onto the skin. The medicine is absorbed into the body slowly and continuously. Hormone treatment can be given by skin patches.

All **systems** have these three elements:

The Manufacturing System

The first **system** we can consider is the whole manufacturing process.





It has each of the three elements, which break down as follows:

The inputs include (in no particular order):

- Data on diseases.
- Specification for the new medicine.
- Money (capital) to pay for energy, equipment, raw materials and employees.
- Expertise of the workforce.
- The technology required to make the product - precision machinery.
- Raw materials.
- Energy source.
- Training requirements of the workforce.
- Policies that govern what is allowed (e.g. the regulations from the Medicines Control Agency).

The processes include (in no particular order):

- The manufacturing cycle itself - converting raw materials into medicines.
- Production systems - the layout of the factory and how equipment is grouped and linked.
- Checking system to ensure the medicine is being made to specification.
- The scale of production - how much medicine is produced and at what rate.

- Whether products are manufactured continuously, or in small or large batches.
- Organisation of the company to maximise productivity and profitability.
- Control of 'quality' of the medicines.

The outputs include (in no particular order):

- The medicines themselves - for example packets of **tablets** or tubes of **cream**.
- By-products as waste - the amount and type of this will vary according to the product; many organisations now recycle this waste.
- The means of storing and transporting the medicines to be distributed and sold.

Systems of Pharmaceutical Manufacture

The tracking system
The tracking **system** is an integral part of the manufacturing system. The safety of the medicines is extremely important. Therefore, it is essential that any problems that may occur can be traced. This can be done more easily if the medicines are made in batches.

Batch production
By making the medicines in batches, it is possible to identify exactly when and where a particular sample was made. Also, it is easy to find all the other medicine that was made in the same batch.

Recording the progress of a batch
There are tests carried out at each stage in the production of a batch. These are to check that the medicine is being made correctly and that the manufacturing process is meeting the specification described in the licence. The tests may include:

Physical

- testing its compressive strength
- weighing it
- measuring the density

Chemical and Biological

- testing the purity
- testing its solubility

The tests are carried out on a batch as it passes through the manufacturing system within the company. The suppliers also check the raw materials for each batch. The results of all these tests are recorded in a detailed register. This ensures that the tests take place and it provides the means of tracing any problems. The system requires staff responsible for a particular stage to:

- Carry out the tests put a time and date stamp in the register.
- Ensure that the results are within allowed tolerances.
- Attach the register to the batch.
- Sign the register showing that the checks have been made.

If there is any problem with that batch at a later date, then the source of the problem can be traced through the register.

SAFETY

Many of the processes in the company require specialist safety clothing. Its main purpose is to protect the workers. Often they wear masks to cover their nose and mouth **so that they don't inhale the dust from tablets**. They may also wear gloves and overalls to cover their skin and clothes. They wear safety glasses and ear defenders in areas where there is heavy or fast moving machinery.

There are also special clothes to keep the manufacturing environment clean and prevent contamination of the product by the operators. They wear nets over hair and beards and put plastic covers over shoes and trainers.

IT systems

Pharmaceutical companies invest heavily in the latest technology. This allows them to develop new, high quality products quickly.

Both Pharmaceutical Research organisations and Engineering houses designing and building facilities use Knowledge Management Systems to store their technical know-how, allowing easy retrieval and global sharing of data.

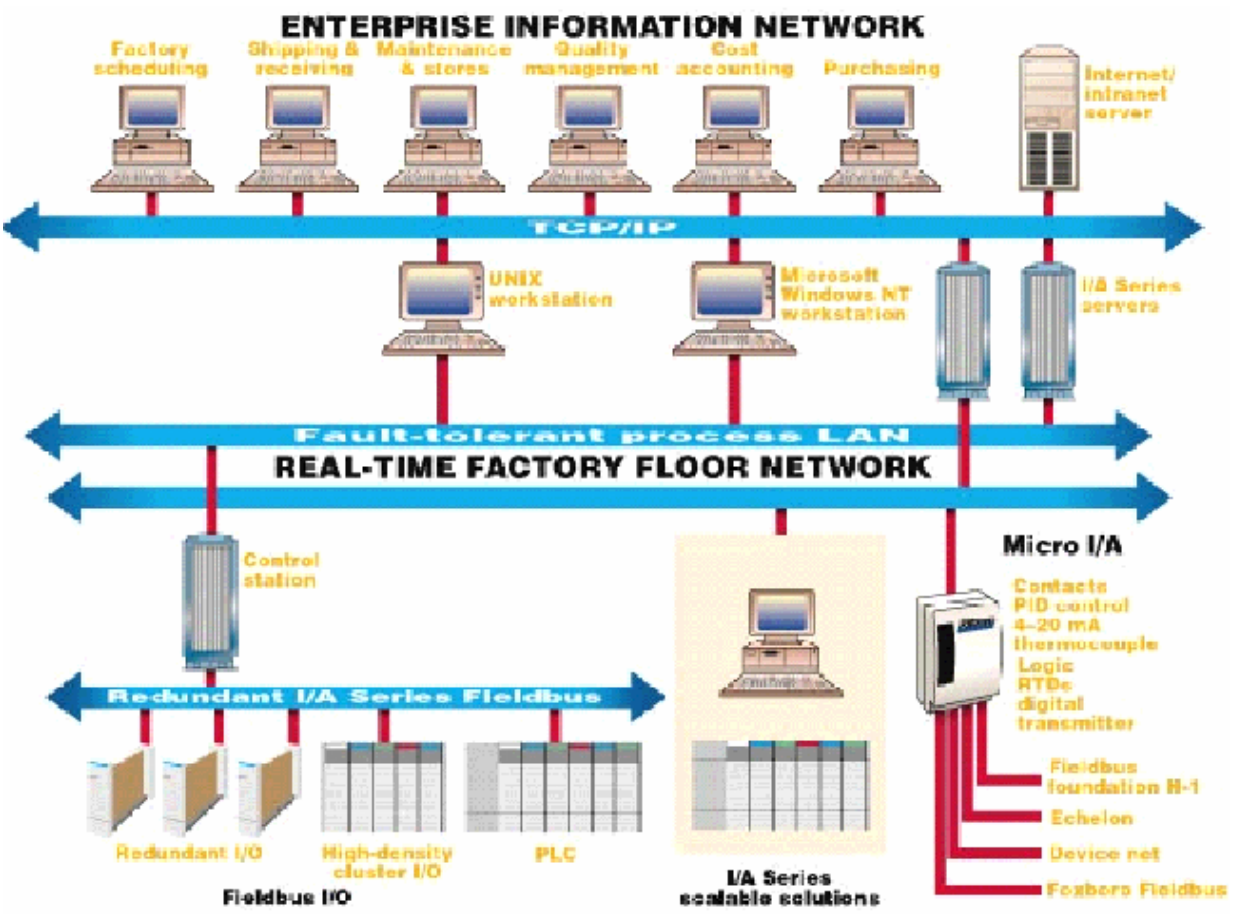
Computer based 3D models are used in detailed designing of Pharmaceutical facilities to ensure that all building and process plant items fit first time. The virtual model allows operators and engineers to 'walk through the facility' to check the design works and meet the needs of the operators. Behind the virtual

plant an engineering database holds details of all the parts, which are used to create construction drawings and material orders for plant erection.

Research teams also use computers to generate new molecules. To combat a particular disease, these molecules have to have the right shape and chemical properties. Having generated some new molecules, the scientists can use computer models to screen them. During the screening, they pick out the ones that are likely to have the right properties.

Using the computers, they can generate and screen up to 10,000 new molecules a year. Without computers, it would take up to ten years to generate and screen this many molecules.

This area of a factory was designed using 3D models on a computer.



Delivery systems for medicines

Technologists have created many large-scale systems to help in the manufacturing process. Less obvious than these is the work they have done on delivery systems. Again, problem-solving expertise is vital.

One example is the inhaler. The medicine is released in a fine spray or a powder and passes directly into a patient's lungs. This allows asthma sufferers to get fast relief from breathing difficulties.

A dry powder inhaler.

Control systems

Throughout the manufacturing process, there is a need for control systems. These may be automated or use human judgement. They are to check when part of the process is complete and that everything is being made correctly. For example, there are:

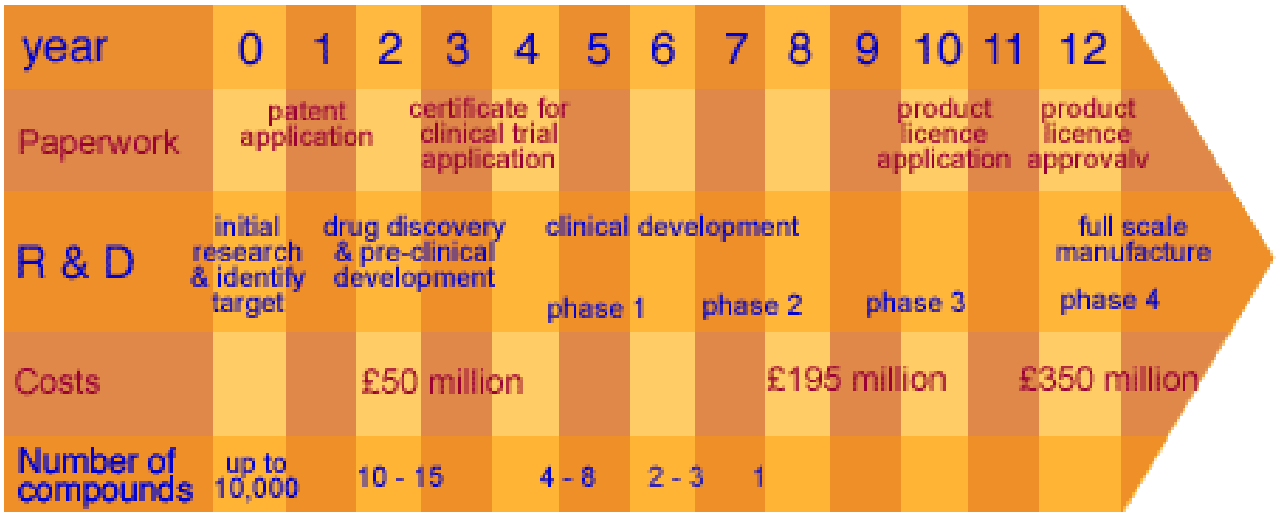
- Counters to ensure the correct number of **tablets** go in a container.
- Cameras that 'check' if **blister** packs of **capsules** are full.
- Electronic weighbridges to ensure that cartons are full of tubes of **creams**.
- Devices that detect unwanted microscopic particles of metal in tablets.
- **Optical sensors** to check that bottles have been filled to the proper levels.
- pH sensors to check acidity.

Technological systems

There are many technological **systems** that make up the essential parts of manufacturing machinery. These use mechanical, electrical, microelectronic, hydraulic and pneumatic components to control and automate the processes.

The development of a new medicine

The industry is constantly developing new medicines. It invests about $30m a day in Research and Development (R&D). This is more than any other manufacturing sector and accounts for about a quarter of the money spent on R&D in the UK.



Discovery Research

A nutraceutical / pharmaceutical company chooses a disease which needs treatment. The scientists investigate its causes and effects. They then look for **therapeutic** compounds that might treat the disease. These might be extracted from a plant or found in their database of compounds. However, these days, many new molecules are generated on a computer.

All the new molecules are screened using biological techniques or computer models. During the screening, scientists can assess whether the molecule is likely to have the desired effect and how safe it might be. As soon as a molecule looks promising, it is patented. This prevents other companies from freely using the same molecule for 20 years.

Preclinical development

The promising compounds are then made up in small quantities and studied in the laboratory. Initially, they will be tested on **cell cultures**. These are collections of living cells that respond as though they were part of an animal. The scientists can determine if the molecules are **toxic** and if they have any therapeutic effects.

Eventually, after extensive testing in the laboratory, a few molecules will prove to have the right properties. These will be tested on animals. These tests can reveal new information about the effects of the molecule in a living body. Before a new compound can be given to humans, much work has to be undertaken to determine:

- Whether it is likely to be effective.
- Whether it is acceptably safe.
- Whether it is sufficiently stable.
- How it is going to be absorbed and excreted by the body.

The data from the preclinical tests are used to apply for a certificate to conduct clinical trials. In the UK, this is issued by the Medicines Control Agency (MCA). Independent medical and scientific experts review the large amount of data. They have to be certain that the medicine will not cause

undue harm to people who are already ill.

Clinical trials - phase I

Phase I trials. This is the first time the new substance is administered to humans; usually the trial is conducted on a small number of healthy, informed volunteers under the close supervision of a doctor. The purpose is to determine if the new compound is tolerated by the patients' bodies, and behaves in the predicted way. The initial dose of the medicine will be as low as possible, but enough to obtain the required information.

Clinical trials - phase II

Phase II trials. These are the first tests in which the illness is actually treated. A group of approximately 200 informed patients is given the medicine. The scientists monitor their progress. They use the results to determine that the medicine works and to check that it does not produce unacceptable side effects. They will also use a control group who are given a placebo. This is to measure how much better the patients feel because they think they are being treated. This has to be taken into account when calculating the effectiveness of the real medicine

Clinical trials - phase III

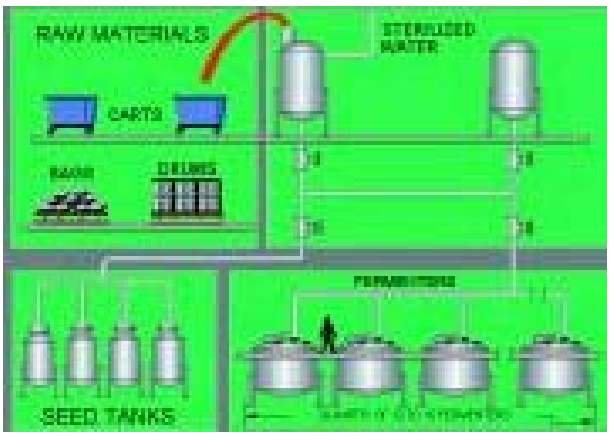
Phase III trials. Now the trial is broadened to involve many more patients - between 1,000 and 3,000. The group is big enough for the company to use statistics to analyse the results. If the results show that the medicine is effective and acceptably safe, the data are presented to the licensing authorities for a commercial licence.

Clinical trials - phase IV

Phase IV trials. This is a surveillance operation once the medicine is on the market. The medicine is made available to doctors, who start prescribing it. The effects can be monitored on thousands of patients to help identify any unforeseen side effects.

It takes up to 12 years to develop a new medicine. Each year, a company's research teams may generate about 10,000 new molecules. These are screened and tested and only one or two will get as far as being given a licence. Only one in seven of these licensed medicines goes on to be a commercial success.

The diagram above shows the progress of a new medicine from discovery, through development to launch.



Primary manufacture

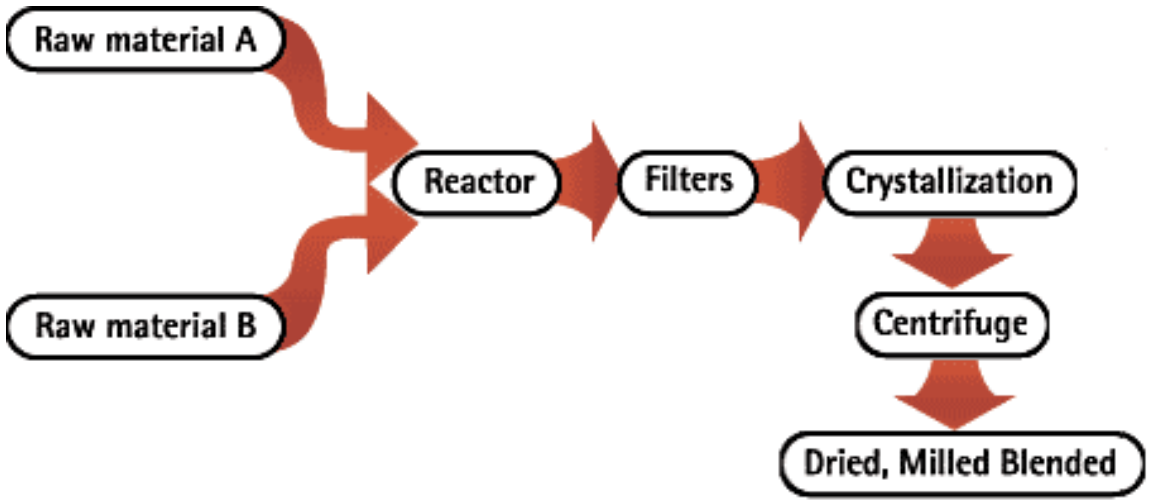
The first stage of making a medicine is to manufacture the active ingredient. We call this stage the **primary manufacture**. The active ingredient will normally make up a small proportion of the final medicine. However, it is the part that will actually make the patient well again.

There are two main ways of developing the active ingredient:

- chemical technology
- biotechnology.

Chemical technology

Primary manufacture often involves chemical reactions to create new molecules. There can be many stages to these reactions. The diagram below shows a simple example in which two ingredients are reacted together. One of the products of this reaction is the active ingredient. However, there are other products as well. The chemists need to isolate and purify the active ingredient using a variety of techniques.

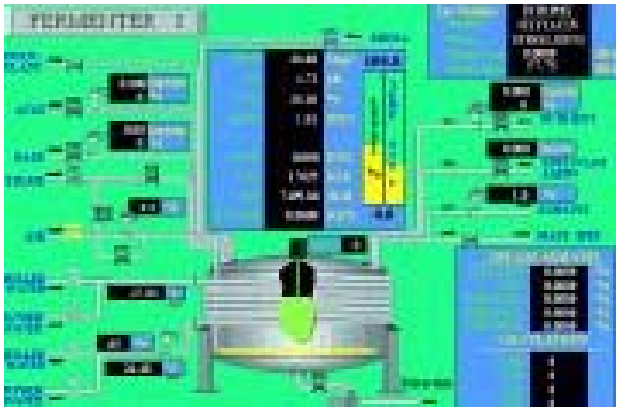


In an example, the active ingredient is in a solution so the mixture can be **filtered** to remove any unwanted residues. The active ingredient will then **crystallise** when the solvent is allowed to evaporate. Sometimes there will need to be more stages before a completely pure sample is produced.

Over the last two decades, there has been an increasing use of biological techniques rather than chemical ones. This is called **biotechnology**.

Inspecting a fermentation vessel used in the manufacture of a medicine

Biotechnology



We can define **biotechnology** as the industrial use of biological material. This means that living materials are used in the manufacture of ingredients. It started when penicillin was extracted from the mould Penicillium notatum in the 1930s. More recently, scientists have modified the genes of **bacteria** so that they can produce useful proteins. By the early 1980s, there were bacteria making human insulin and human growth **hormone**. We call this technique **genetic engineering**.

Genetic engineering

Genetic engineering allows scientists to introduce new genes for useful proteins into the **DNA** of cells. The cells may be bacteria, fungi or cultures of animal cells. The modified cells can be grown on a large scale to produce proteins in industrial quantities. These products are called biopharmaceuticals. They can be **vaccines**, hormones, **enzymes** or monoclonal antibodies. Monoclonal antibodies help to prevent rejection of transplants and can treat and diagnose some cancers.

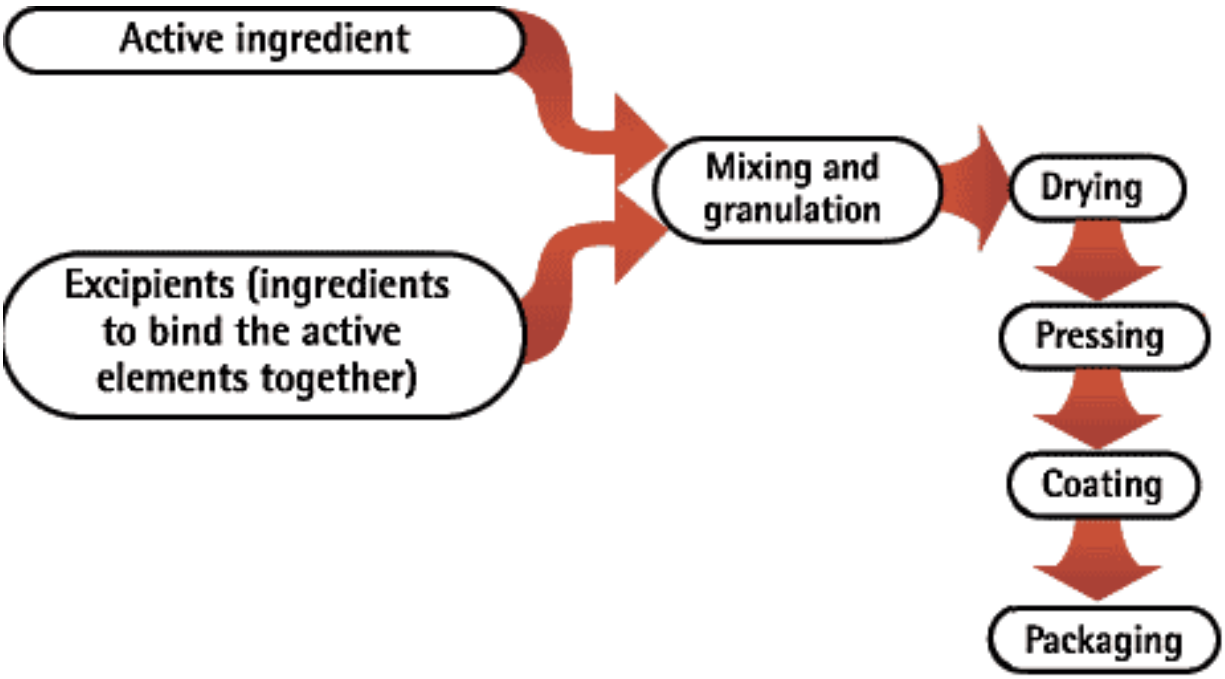
Making biopharmaceuticals

The production of biopharmaceuticals is similar to the **primary manufacture**. The raw materials are usually the cells or micro-organisms and the culture medium in which they grow. The reactor is usually a fermenter where conditions are carefully controlled to optimise activity. The product is extracted using a series of **filters** and **centrifuges** and purified by **chromatography**. The active ingredient is usually provided in **vials** as a solution or as a freeze dried powder. It is then ready to be formulated in **secondary manufacture**.

The Human Genome Project is the enormous job of mapping the complete Human Gene. It is changing our understanding of diseases and their causes. Most importantly, with the help of **biotechnology**, it may allow us to cure them.

Using the active ingredient

The active ingredient is the output of the primary manufacturing stage. However, it is not in a suitable form to give to a patient. It has to be turned into a medicine. This is done in secondary manufacture.



This flow diagram shows the **secondary manufacture** of **tablets**. A range of different medicines can be made in secondary manufacture.

Secondary manufacture

In **secondary manufacture**, companies must follow a strict code of **good manufacturing practice (GMP)**. The active ingredient is turned into a medicine by mixing it with other substances. These are called **excipients** and they make up most of the volume of a medicine. Although they have no active role in curing a patient, they allow the active ingredient to be made into a medicine, such as a **tablet**.

There are a number of different ways of formulating a medicine.

Manufacturing Tablets

The six basic stages in manufacture are:

Inputs

1 delivery of ingredients to the factory
2 checking that the ingredients meet the required specification

Processes

3 mixing and granulation
4 drying
5 pressing
6 coating.

Receiving the ingredients.

The company's suppliers deliver the ingredients to the factory. The ingredients are usually powders, although they can be crystals or very small, spherical granules.

Checking ingredients.

The ingredients for the tablets are checked very carefully:

- Active ingredients are identified chemically.
- Some ingredients are weighed.
- The ingredients are analysed to check they match the specification.
- The solid ingredients are passed through a sieve to check nothing unwanted has got in.

Receiving goods.

Top end of a granulator.

Secondary manufacture

Mixing and Granulation.

The powdered ingredients are then placed inside a mixer like a large food mixer. They are mixed to ensure that the active elements are combined uniformly with the **excipients**. Unless this process happens thoroughly, one tablet may have too much activity and another none at all. Water is then added to granulate the mixture. The water binds the powders together to form granules (like instant coffee). This stops the powders from separating (or demixing) whenever the mixture is moved.

CONTROL POINT

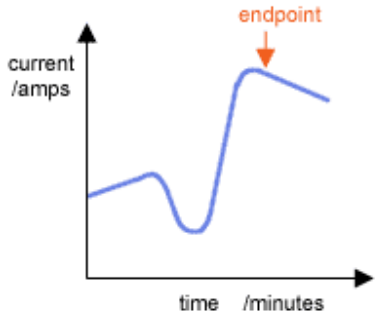
The progress of this process is monitored by checking on the current drawn by the motor that powers the mixing blade, or impeller. This gives a measure of the amount of turning force (**torque**) it is using to mix and granulate the ingredients. When the process is nearing its end, the ingredients are uniformly mixed and have formed into granules. The torque required to turn the granules is greater, and the motor draws a bigger current. An average time for this part of the process is 10 minutes.

Drying.

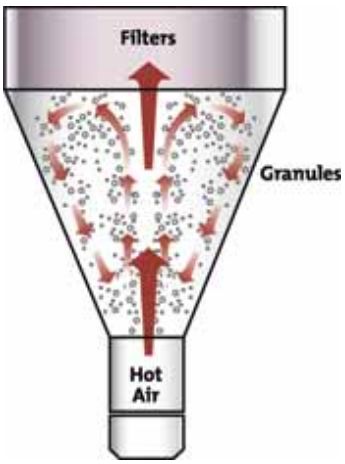
The granules are dried in a fluid bed drier. This has a large fan facing upwards. It creates giant currents of heated air. The air picks up the granules and carries them up in a warm flow. The granules fall down and are picked up by more hot air.

The granules pass from the fluid bed drier through a sieve. This breaks up the oversized granules and ensures the size is uniform. The powder of fine granules is then ready to be pressed into tablets.

The outside of a fluid bed dryer.



Graph of current against time for the granulator motor.



Pressing.

The tablet press is a high-speed mechanical device. It 'squeezes' the ingredients into the required tablet shape with extreme precision. It can make the tablet in many shapes, although they are usually round or oval. Also, it can press the name of the manufacturer or the product into the top of the tablet.

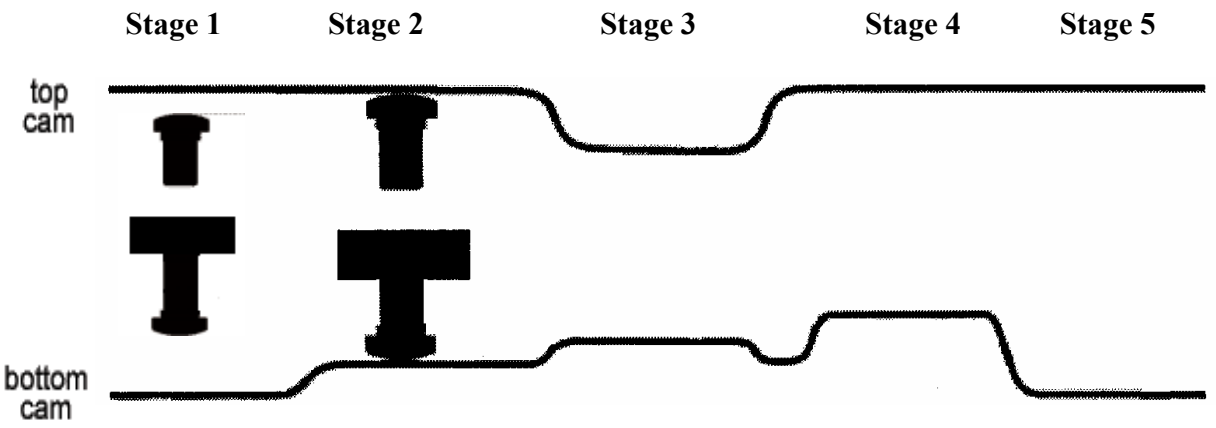
Each tablet is made by pressing the granules inside a die made of hardened steel. The die is a disc shape with a hole cut through its centre. The powder is compressed in the centre of the die by two hardened steel punches that fit into the top and bottom of the die.

The punches and dies are fixed to a turret that spins round. As it spins, the punches are driven together by two fixed cams - an upper cam and lower cam. The top of the upper punch (the punch head) sits on the upper cam edge. The bottom of the lower punch sits on the lower cam edge.

The shapes of the two cams determine the sequence of movements of the two punches. This sequence is repeated over and over because the turret is spinning round.

The force exerted on the ingredients in the dies is very carefully controlled. This ensures that each **tablet** is perfectly formed. The turret holds up to 75 dies and pairs of punches. It spins extremely fast and can produce up to 600,000 tablets per hour. Because of the high speeds, they need very sophisticated lubrication **systems**. The lubricating oil is recycled and **filtered** to ensure a continuous supply.

Sequence of punch movements - roll your cursor over the stages



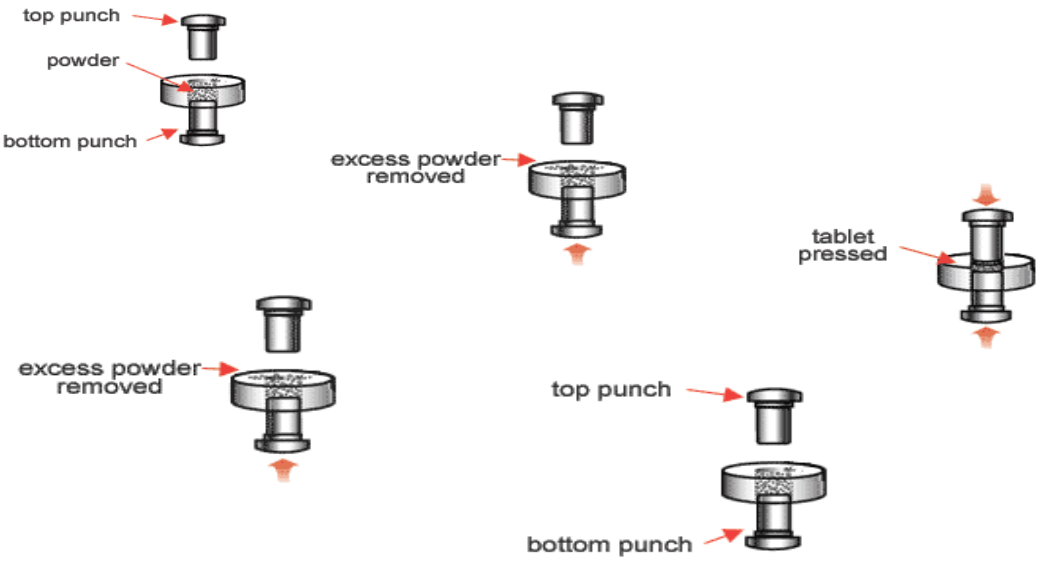
Stage 1 Top punch is withdrawn from the **die** by the upper cam.
Bottom punch is low in the die Powder falls in through the hole and fills the die.

Stage 2 Bottom punch moves up to adjust the powder weight - it rises and expels some powder.

Stage 3 Top punch is driven into the die by the upper cam.
Bottom punch is raised by the lower cam.
Both punch heads pass between heavy rollers to compress the powder.

Stage 4 Top punch is withdrawn by the upper cam.
Lower punch is pushed up and expels the **tablet.**
Tablet is removed from the die surface by the surface plate.

Stage 5 Back to Stage 1.



Inspecting the tablet press.

Turret holding the punches.

Coating

Some tablets are then coated. The coating performs a number of jobs. For example it *can* be to:

- Prevent the tablets cracking or breaking in transit.
- Allow the controlled release of the active ingredient over a longer time than simply allowing the tablet to dissolve.
- Mask the taste.
- Prevent the tablet from breaking up.
- Make the tablet easier to swallow.

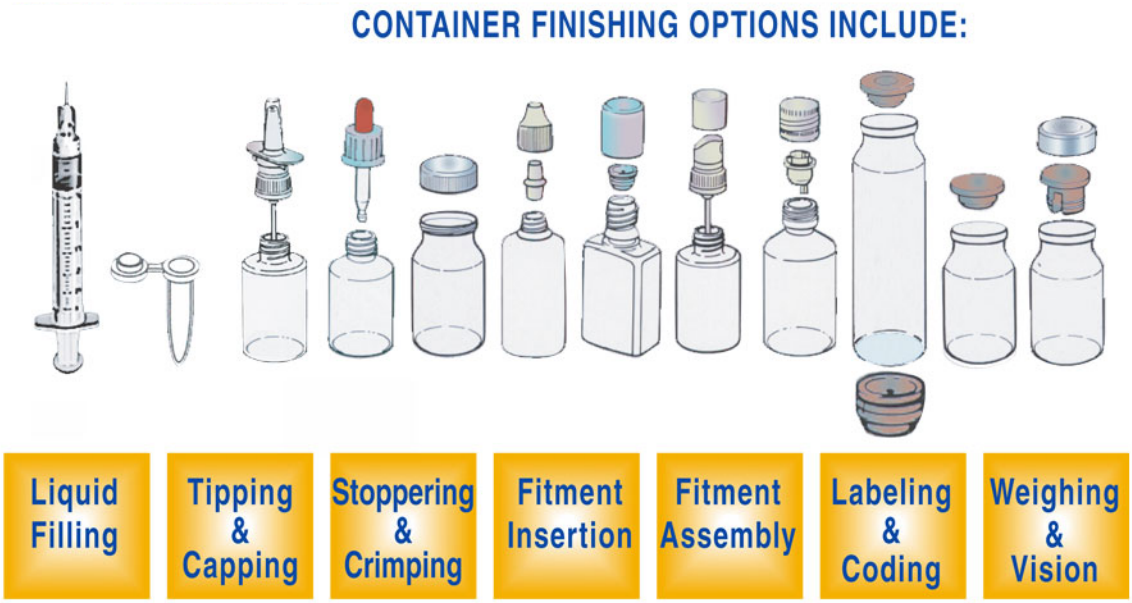
The coating machine is like a tumble drier with nozzles suspended across the width of the drum. The batch of **tablets** is rotated in the drum and the nozzles spray on the coating. Baffles attached to the inside of the drum ensure that every tablet is coated properly.

Once again, the coating process is very carefully controlled. This is to ensure that the coating on every tablet is even and is the correct thickness. There could be half a million tablets in the coating machine. So an error could be extremely expensive.

The production of the tablet is now complete. It is ready to be tested and then packaged before leaving the factory.

A coating machine.

Packaging



Nutraceutical and Pharmaceutical manufacturers have to package their medicines before they can be sent out for distribution. The type of packaging will depend on the formulation of the medicine. However, we will look at a case study of putting **tablets** into '**blister** packs'.

A blister pack.

'Blister packs' are a common form of packaging used for a wide variety of products. They are safe and easy to use and they allow the consumer to see the contents without opening the pack.

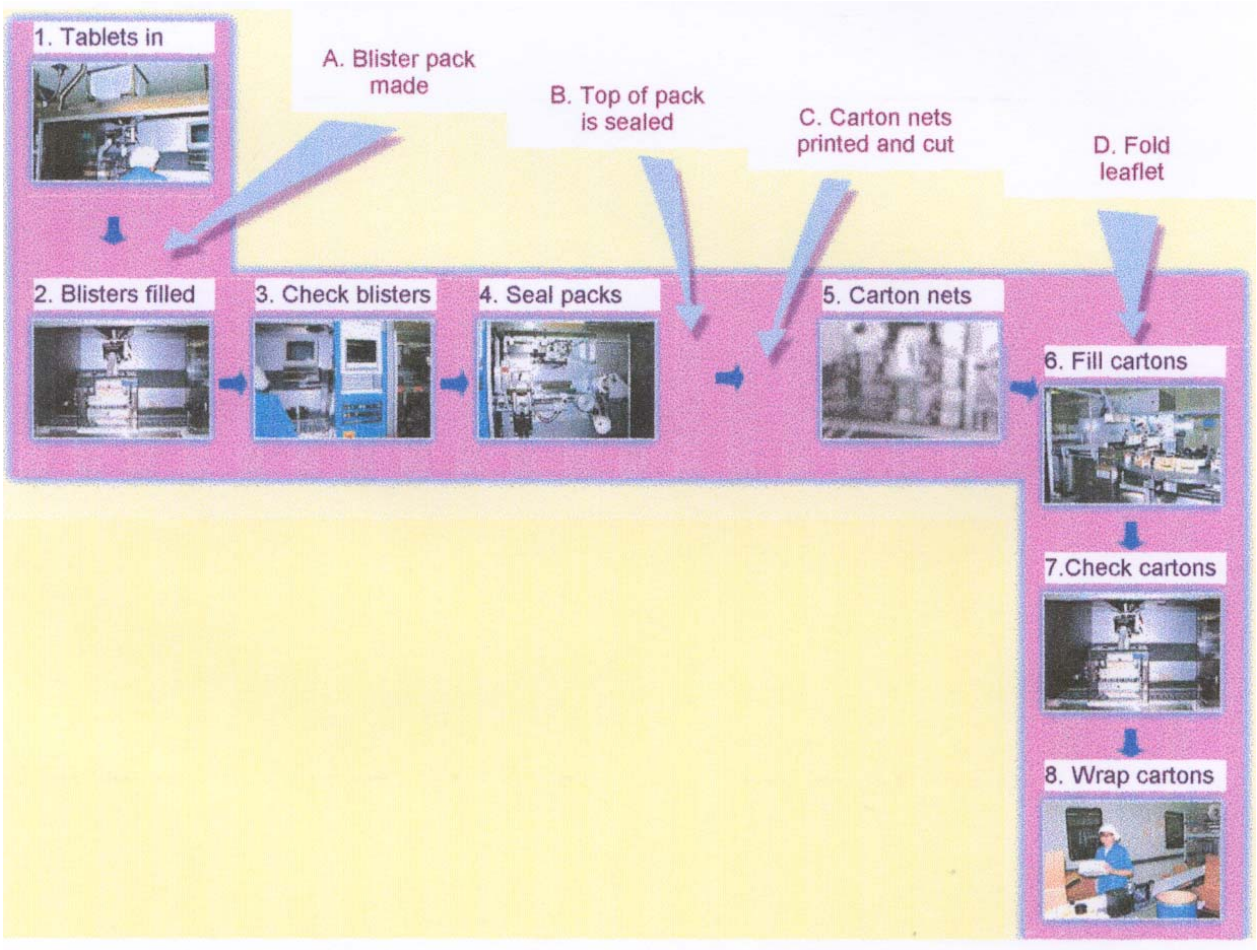
Many nutraceutical and pharmaceutical companies use a standard size of blister pack. This saves the cost of having to make different tools and of having to change the production machinery between products. Capsules can also be packaged in a similar way.

Sometimes the pack will be perforated so that individual tablets can be detached. This means that the expiry date and the name of the product have to be printed on each part of the package.

The **blister** pack itself must remain absolutely flat as it travels through the packaging processes, especially when it is inserted into a carton. This poses interesting problems for the designers. Extra ribs are added to the blister pack to improve its stiffness.

Stages in the packaging process

The packaging takes place in a sequence like a production line. Tablets are taken in at one end and boxed up cartons of **blister**-packed **tablets** pass out at the other end. There are some extra inputs to the **system** along the way. These are shown as letters in the sequence.



1. The tablets are brought to the packaging line.

The **tablets** are brought in 80kg bulk bags and suspended over the line. The base of the bulk bag is opened to allow the tablets to trickle out.

2. The tablets are placed in the 'blisters'.

From the hopper, a series of vibrating tracks shake the **tablets** to separate them. The separated tablets are placed into the blister cavities.

3. A check is made that all the blisters are full.

CONTROL POINT: It is vital to ensure that each blister cavity is filled with a tablet.

A camera system monitors each blister. Incomplete packs are automatically ejected from the packaging line.

4. The packs are sealed and separated with an expiry date.

The separate blister packs are still attached to one another in a long continuous strip. Therefore, they must be cut into individual units, using a guillotine.
Many medicines have to carry their expiry date and batch numbers. An embossing tool prints this onto the pack. Again, optical control systems determine the position of the blister pack as it passes the printing head.

The blister packs are stored vertically in a stack.

The blister packaging is now complete.
The blister packs are collected ready to go into cartons.

5. The flattened carton nets are opened up.

The cartons come as flat sheets. This is the **net** of the carton - ready to be folded into shape. The sheets are loaded into a mechanical feed mechanism. A **pneumatic gripper** lifts the top surface of the carton, opening it out into three dimensions. The sides of the carton are folded round and closed.

6. The packs and a leaflet are inserted into each open carton.

The required number of blister units is dispensed from a vertical stack and held using a 'finger gripper'. It's here that the flatness of the packs is imperative. Any bent packs will not go into the cartons and will jam the machinery.

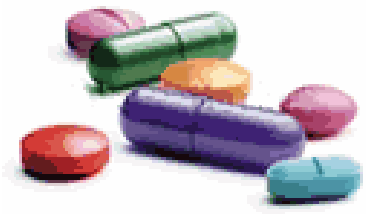
The leaflet is then 'wrapped around' one end of the blister packs and the whole bundle is inserted into the open end of the carton. Batch number and expiry date are embossed on the carton at this point. This is then closed using a mechanical linkage.

7. A weighbridge checks that each carton is full.

CONTROL POINT
The cartons are weighed very carefully to ensure that they contain the correct number of blister packs and a leaflet. If any part of the contents is missing, the carton will be underweight and is automatically ejected from the packaging line.

8. Units of 20 cartons are band-wrapped.

The cartons containing the **tablets** are put into units of 20. These are then encircled by a plastic band, which is tightly wrapped around and cut to make neat easy-to-handle bundles of cartons.
These are put into boxes by hand which are then stacked on aluminium pallets. The boxes of cartons of tablets are shipped from the company ready to be distributed.



What makes nutraceutical and pharmaceutical manufacture different?

All of manufacturing industry has an overriding concern for quality. This means they want to make products 'right first time' without any flaws or defects. The drive to maintain this quality is called Total Quality Management (TQM). There are three main aspects of TQM that are distinctive to the nutraceutical and pharmaceutical industry.

1. The long development time.

Once a promising molecule has been found, it can take up to 12 years to the launch of the medicine. This is much longer than, say, the development of a new car. However, it is essential to allow the company to ensure that the medicine is acceptably safe.

2. The licence and the production processes.

The manufacture of a motor car can be changed once it has started. However, in the pharmaceutical industry a licence has to be granted before a medicine can be produced. Its issue depends on the production process. Therefore, once the licence has been issued, it is very difficult to change the process. This means that the production process must be carefully planned at the very beginning.

3. An overriding concern for safety.

This can be seen by the use of strict **quality control** systems. These exist at all stages in the manufacture and trialling of the new medicine and include:

- Checking the safety of a medicine through extensive trials.
- A **system** for tracking each stage in the production of a batch.
- Heavy investment in training.

Pharmaceutical companies devote a lot of time to training. They encourage their staff to take responsibility for their work. They can't rely on someone else making up for their mistakes. They know that their contribution has to be perfect for the medicine to be as safe as possible and for the company to succeed.

Conclusion

Nutraceutical and Pharmaceutical manufacture is a high technology process. As well as relying on the skill and knowledge of their employees, pharmaceutical companies use high precision and efficient control systems. They are major employers in this country and contribute significantly to the economy. The industry seems to have a good future but, as with anything successful, it cannot be complacent and remains a dynamic, developing industry.

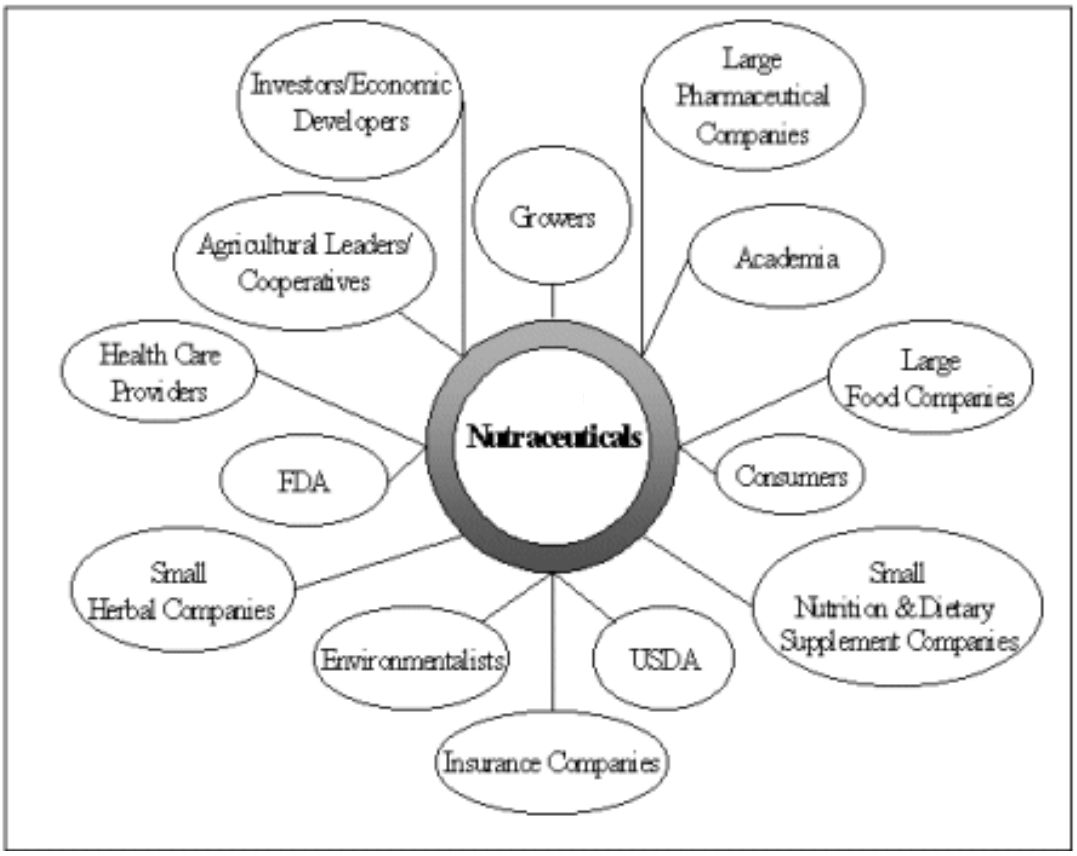
WHAT ARE NUTRACEUTICALS?

Nutraceuticals (often referred to as phytochemicals or functional foods) are natural, bioactive chemical compounds that have health promoting, disease preventing or medicinal properties.

Nutrition as medicine, integrating diet and nutraceuticals.

"You are what you eat" is no longer a saying, it's a science. How can we make our patients healthier through nutrition? Are supplements necessary? What are nutraceuticals and when should they be used?

Nutraceuticals or functional foods are terms used to describe natural foods that demonstrate physiological benefits and/or reduce the incidence of chronic disease.



HEALTH FOOD STORE SUPPLEMENTS VS. NUTRACEUTICALS:

The following comparison table between health store supplements and nutraceuticals shows you why we offer our clients only certified nutraceutical products.

Health Food Store Supplements	Nutraceuticals
• Food grade processing. • 300% concentrate. • Can be a stimulant to digestion (carminative) therefore often recalled by the Health Protection Branch.	• Pharmaceutical grade processing. • 3,000% concentrated. • FDA approved or TGA approved.
• Bulk purchased from a second party. • Not assayed, therefore not inspected.	• Batch purchased from prime source. • Assayed before accepted. • Certificates of analysis available upon request from independent laboratories. • Safe from GMO's (genetically modified organism).
• Packaged with binders (additives). • Processed under high pressure with solvents that are inflammable. • Heat degrades viability. • The use of CFC's and CO_2 creates an acidic pH.	• Packaged with low pressure enzyme catalyzed, inert pH. • No thermal degradation. • Phytosols used for extraction--nonflammable and non-toxic.
• Sold to the public. • Meet food grade requirements, i.e. GRAS (generally regarded as safe), not pharmaceutical requirements.	• Sold only to health practitioners who must be licensed by a board or approved by examination.
• Sold over the counter, therefore can be purchased without any liability to business.	• By professional sales only. Not sold to the public directly.
• Supplemental--to enhance dietary deficiencies (not tested).	• Conditional--to treat specific health conditions, therefore requires a trained health professional.
• Recommended by an unlicensed employee.	• Recommended by a health professional who has studied and passed exams for professional use.
• Suppliers are profit oriented. • Use non-expensive recycled materials, e.g. oyster shell or chicken shell for calcium.	• Suppliers are profit *and* health oriented. • Suppliers sole purpose is to assist health professionals to optimize their patients' health.

• Non-specific research. • General articles.	• Specific clinical research ongoing. • Universities and several teams of Doctors.
• Trends, fads, hype. • Mass marketing.	• Constant association upgraded information. • Current clinical research by health professionals. • Results from projects. • Individual doctor studies.
• Non-certified. • Buyer beware standard.	• Certified organic. • Guaranteed uncontaminated sources.
• No “disintegration” standards. • Could be indigestible.	• Meets standardized USP “disintegration” standards. • Disintegrates within 40 minutes at body temperature.
• Non-patented processing.	• Patented processing method. • Preparations are stabilized for storage and viability.
• No Drug Identification Numbers (DIN).	• DIN or DIN numbers pending. • DIN number applications are current with FDA requirements.